Evaluation of Sweat Production by Pilocarpine Iontophoresis: A Noninvasive Screening Tool for Hypohidrosis in Ectodermal Dysplasia

Surupa Basu · Monjori Mitra · Apurba Ghosh

Received: 24 December 2012 / Accepted: 25 April 2013 / Published online: 15 May 2013
© Association of Clinical Biochemists of India 2013

Abstract Ectodermal dysplasia (ED) is a genetic disorder affecting the skin, hair, nails, teeth and sweat glands. The clinical presentation is heterogenous; however, hypohidrotic (reduced sweat) ectodermal dysplasia (HED) being the commonest. Also known as anhidrotic ED, sweat glands are sparse or rudimentary, leading to dysregulation of body temperature and episodes of uncontrolled hyperthermia due to reduced sweating. Of the many aids to document hypohidrosis in HED, we present here the technique of pilocarpine iontophoresis to induce, collect and measure sweat. Evaluation of sweat generated (against normally obtained values) is a non-invasive alternative to establish hypohidrosis in disorders such as HED. This augments clinical decision levels to plan skin biopsy for confirmation of diagnosis and facilitates patient management and early discharge. We present two cases of HED that were primarily diagnosed with sweat gland dysplasia using pilocarpine iontophoresis, and later confirmed with skin biopsy findings.

Keywords Hypohidrotic ectodermal dysplasia · Pilocarpine iontophoresis · Sweat test · Hyperthermia

Introduction

Ectodermal dysplasia (ED) is a heterogeneous group of genetic disorders wherein the ectoderm of certain areas fails to develop normally [1]. It is characterized by a constellation of findings involving defects of the teeth, skin, or appendageal structures including hair, nails, and eccrine and sebaceous glands. Hypohidrotic ectodermal dysplasia (HED) manifests as a triad of defects: hypohidrosis (anhidrosis) of sweat glands, anomalous dentition, and hypotrichosis. Incidence of EDs is estimated to be 7 in every 10,000 live births [2].

Specific diagnosis of HED is done by showing paucity or complete absence of sweat glands from palmar or scalp biopsy. A non-invasive, simpler, and quicker method to screen patients for HED is the demonstration of reduced sweat production, by performing sweat measurement. In this report, we discuss two cases of clinically suspected HED that were initially investigated for reduced sweat production using the method of pilocarpine iontophoresis followed by confirmation of diagnosis with skin biopsy findings. The report has been approved by the Institutional Ethical Committee board.

Case Reports

Case 1

An 8 month old female infant with delayed neuro-developmental milestones, born of a non-consanguineous marriage, was admitted with complaints of high grade fever of unknown origin for the past 12 weeks. She had a history of recurrent attacks of fever since birth, for which she was hospitalized several times. Fever one of the most frequent

S. Basu (✉)
Department of Biochemistry, Institute of Child Health,
11, Dr. Biresw Guha Street, Kolkata 700017, India
e-mail: surupa.basu@rediffmail.com

M. Mitra
Pediatric Medicine, Institute of Child Health, 11,
Dr. Biresw Guha Street, Kolkata 700017, India

A. Ghosh
Institute of Child Health, 11, Dr. Biresw Guha Street,
Kolkata 700017, India

symptoms of diseases in children, points diagnostically to an infection. The first line of investigations was a septic screen, which was negative, and infectious cause was excluded. The patient's mother had observed that her child did not sweat in spite of high ambient temperatures. She would become very irritable during summer and had to be pacified by bathing or sponging. Causes of hypohidrosis were investigated for such as hyperthyroidism, diabetes mellitus; others like congenital insensitivity to pain with anhidrosis, ichthyosis, cholinergic urticaria, exfoliative dermatitis etc. were excluded by clinical examination and history. Though there were no other features of ED (hair was not sparse, no abnormal dentition or complaints of abnormal pain/temperature sensation), dyshidrosis (ED subgroup 4) was considered and pilocarpine iontophoresis (to measure sweat production) was carried out at the biochemistry laboratory. A dermal biopsy was outsourced to a local laboratory for confirmation.

Case 2

A 6 year old male child had presented to the general outdoor pediatric clinic with complaints of reduced sweat production, dry scaly skin and recurrent fever. He was born of a consanguineous marriage, was the first child in the family, with a normal sibling and no other family members having similar symptoms. There was a high suspicion of congenital HED (ED sub group 1–2–4) as the child had classical features of coarse sparse thin lightly pigmented hair, frontal bossing, scanty eyebrows, absent eye lashes and oligodontia (only two upper incisors, no teeth in lower jaw) (Fig. 1). He had a history of two episodes of pneumonia, repeated nasal crusting and bleeding, especially in the summer season. Sweat analysis was done using pilocarpine iontophoresis.

Method

Pilocarpine Iontophoresis

Pilocarpine nitrate is a cholinergic agent that binds to muscarinic receptors of eccrine sweat glands and induces sweat production. It is imbibed into the sweat glands in the forearm of the patient by iontophoresis i.e. using a small electrical current to push the chemical agent through the skin (Fig. 2). The sweat is collected in a piece of pre-weighed filter paper (of fixed dimensions) which is placed on to the area of iontophoresis and bandaged using a cling film. The patient is asked to remain outdoors for exactly 30 min. The filter paper is retrieved and carefully weighed on a sensitive analytical (0.001 g precision) balance to determine the weight of sweat collected.

Fig. 1 A child of hypohidrotic ectodermal dysplasia (Case 2). Mark the classical features of sparse, thin and lightly pigmented hair, frontal bossing, protruding lips, scanty eyebrows, absent eye lashes and absence of teeth in the lower jaw

Fig. 2 Pilocarpine iontophoresis being conducted on a patient of suspected hypohidrotic ectodermal dysplasia

We are routinely performing a validated indigenous sweat chloride analysis for the diagnosis of cystic fibrosis [3]. In these cases, the procedure was utilized to diagnose suspected hypohidrotic ED by measuring the amount of sweat generated.

Result

Both cases had a minimal sweat yield (average from two consecutive procedures) of 16 and 22 mg; when compared with 30 age-matched controls who went through the sweat test for unrelated reasons and had a mean sweat yield of 224 mg (SD $\pm$ 0.04)/30 min. The low sweat yield documented hypohidrosis in both cases. Skin biopsy reported findings of redundant hair follicles and paucity of sweat glands and confirmed diagnosis.

Discussion

A child in the pediatric ward can present with hypohidrosis from several causes [4]. Sweating, although present, is greatly deficient, leading to episodes of hyperthermia. Patients present with pyrexia and complaints of reduced sweating.

One common cause of hypohidrosis is ED with affected sweat glands. ED may manifest singly or in a combination of the following—ED1: trichodysplasia (hair dysplasia), ED2: dental dysplasia, ED3: onychodysplasia (nail dysplasia), ED4: dyshidrosis (sweat gland dysplasia; eccrine sweat glands may be sparse or rudimentary). The strongest diagnostic aid for HED is the clinical presentation of the three cardinal features of hypotrichosis, hypohidrosis and hypodontia [5].

Hypohidrosis can be documented by demonstrating reduced sweating (functional loss due to reduced number of sweat glands) and confirmed with a skin biopsy that shows evidence of paucity of sweat glands.

One qualitative method, which is popularly used to demonstrate reduced ability to sweat, is the assessment of the sweat pore counts. This is done by coating parts of the body with starch and pouring iodine solution and visualizing the areas of sweating where the iodine turns a purple colour [6, 7]. The method has low sensitivity, is cumbersome and the interpretation observer dependent. A quantitative technique is the method of pilocarpine iontophoresis that has been described in this report. This method is accurate and can be easily accessed in centres where pilocarpine iontophoresis is a routine procedure to generate sweat, usually for the sweat chloride estimation. Sweat tests have been shown to rapidly support diagnosis of the HED phenotype, in the presence of other features of ED [7]. Pilocarpine iontophoresis has been used to document minimal sweat production in a young infant with recurrent hyperthermia [8]. Similar utility of the technique has been in the detection of oligohydrosis in children with hyperthermia who were on topiramate therapy [9].

It is a non-invasive test with a short turnaround time, which would help clinicians rule out hypohidrosis if

negative; or facilitate further patient management and decide for the invasive skin biopsy for confirmation, if positive.

Conclusion

Pilocarpine iontophoresis and quantification of sweat production can be a valuable non-invasive screening tool to document hypohidrosis. Early detection helped to effectively manage two pediatric cases of ED with hypohidrosis. The same can also be applied to screen other disorders that present with dyshidrosis, before planning a skin biopsy for confirmatory diagnosis.

References

1. Clarke A. Hypohidrotic ectodermal dysplasia. *J Med Genet.* 1987;24:659–63.
2. Dall'Oca S, Ceppi E, Pompa G, Polimeni A. X-linked hypohidrotic ectodermal dysplasia: a ten year case report and clinical considerations. *Eur J Paediatr Dent.* 2008;9(4):14–8.
3. Kabra SK, Kabra M, Gera S, Lodha R, Sreedevi KN, Chacko S, et al. An indigenously developed method for sweat collection and estimation of chloride for diagnosis of cystic fibrosis. *Indian Pediatr.* 2002;39:1039–43.
4. Morelli JG. Disorders of the sweat glands. In: Kliegman, Stanton, St. Geme, Schor, Behrman, editors. *Nelson's textbook of pediatrics.* 19th ed. Philadelphia: Elsevier; 2011. p. 2286–7.
5. Vinola RK, John JB. Hypohidrotic ectodermal dysplasia: diagnostic aids and a report of 5 cases. *J Indian Soc Pedod Prevent Dent.* 2010;28(1):47–54.
6. Clarke A, Burn J. Sweat testing to identify female carriers of X linked hypohidrotic ectodermal dysplasia. *J Med Genet.* 1991;28:330–3.
7. Rouse C, Siegfried E, Breer W, Nahass G. Hair and sweat glands in families with hypohidrotic ectodermal dysplasia: further characterization. *Arch Dermatol.* 2004;140(7):850–5.
8. Dittmer A, Erler T, Gurski A, Müller P. Hypohidrotic ectodermal dysplasia as the cause of recurrent hyperthermia in a young infant. *Kinderarztl Prax.* 1992;60(8):239–42.
9. Ben-Zeev B, Watemberg N, Augarten A, Brand N, Yahav Y, Efrati O, et al. Oligohydrosis and hyperthermia: pilot study of a novel topiramate adverse effect. *J Child Neurol.* 2003;18(4):254–7.